REMARKS

Claims 28-42, 44-51 and 52-57 are pending in this application. Claims 1-27 and 43 have been canceled without prejudice or disclaimer. Claims 28-42 and 44-52 have been amended. Claims 53-57 have been newly added.

Claims 44-45, 48-49 and 52 are withdrawn from consideration as being directed to a non-elected species. Applicants note that upon allowance of a generic claim, Applicants will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 C.F.R. § 1.141.

Claims 1-27 and 43 have been canceled without prejudice or disclaimer, and claims 28-42 and 44-52 have been amended, for the sole reason of advancing prosecution. Applicants, by canceling or amending any claims herein, make no admission as to the validity of any rejection made by the Examiner against any of these claims. Applicants reserve the right to reassert any of the claims canceled herein or the original claim scope of any claim amended herein, in a continuing application.

Claim 28 has been amended to recite "[a] pharmaceutical composition for parenteral administration comprising a therapeutically effective amount of a protein or polypeptide non-covalently bound to one or more colloidal particles, the one or more colloidal particles comprising approximately 1-20 mole percent of an amphipathic lipid derivatized with a biocompatible hydrophilic polymer, wherein the protein or polypeptide is selected from the group consisting of: (a) Factor VIIa, granulocyte colony-stimulating factor (G-CSF), granulocyte macrophage colony-stimulating factor (GM-CSF), interferon γ, glucagon-*like* peptide 1 (GLP-1) and Copaxone; or (b) proteins or

polypeptides that comprise a consensus sequence of S/T-X-L/I/V-I/V/Q/S-S/T-X-X-E, where X may be any amino acid, and S, T, L, I, V, E and Q have their standard meanings; wherein the protein or polypeptide is not Factor VIII (FVIII), and the protein or polypeptide is not encapsulated in the one or more colloidal particles." Support for claim 28 as amended can be found throughout the specification and claims as originally filed. For example, please *see* page 4, lines 7 and 10-17 of the present specification.

Claims 29-42 and 44-46 depend, either directly or indirectly, from claim 28. Claims 29-42 and 44-46 have been amended to be in a form consistent with U.S. practice. For example, the term "said" has been deleted and replaced with the term "the." Claim 44 has been amended to place it in proper Markush form. No new matter has been added.

Claim 47 has been amended to recite "[a] method for treating a patient suffering from a disease that is known to be treatable with a protein or polypeptide known to effectively treat the disease, comprising administering to a patient in need thereof a pharmaceutical composition for parenteral administration comprising a therapeutically effective amount of the protein or polypeptide non-covalently bound to one or more colloidal particles, the one or more colloidal particles comprising approximately 1-20 mole percent of an amphipathic lipid derivatized with a biocompatible hydrophilic polymer, wherein the protein or polypeptide is selected from the group consisting of: (a) Factor VIIa, granulocyte colony-stimulating factor (G-CSF), granulocyte macrophage colony-stimulating factor (GM-CSF), interferon γ, glucagon-*like* peptide 1 (GLP-1) and Copaxone; or (b) proteins or polypeptides that comprise a consensus sequence of S/T-X-L/I/V-I/V/Q/S-S/T-X-X-E, where X may be any amino acid, and S, T, L, I, V, E and Q have their standard meanings; wherein the protein or polypeptide is not Factor VIII (FVIII), and the

protein or polypeptide is not encapsulated in the one or more colloidal particles." Support for amended claim 47 can be found throughout the specification and claims as originally filed. For example, please *see* page 4, lines 7 and 10-26 of the present specification. Claims 48 and 49 depend directly from claim 47. Claims 48 and 49 have been amended to be in a form consistent with U.S. practice. No new matter has been added.

Claim 50 has been amended to recite "[a] method for treating a patient suffering from a disease that is known to be treatable with a protein or polypeptide known to effectively treat the disease, comprising administering to a patient in need thereof a therapeutically effective amount of the protein or polypeptide selected from the group consisting of: (a) Factor VIIa, granulocyte colony-stimulating factor (G-CSF), granulocyte macrophage colony-stimulating factor (GM-CSF), interferon γ, glucagon-*like* peptide 1 (GLP-1) and Copaxone; or (b) proteins or polypeptides that comprise a consensus sequence of S/T-X-L/I/V-I/V/Q/S-S/T-X-X-E, where X may be any amino acid, and S, T, L, I, V, E and Q have their standard meanings; and one or more colloidal particles comprising approximately 1-20 mole percent of an amphipathic lipid derivatized with a biocompatible hydrophilic polymer, wherein the one or more colloidal particles and the protein or polypeptide are administered separately." Support for amended claim 50 can be found throughout the specification and claims as originally filed. For example, please *see* page 4, lines 7 and 10-26 of the present specification. Claims 51 and 52 depend directly from claim 50. Claims 51 and 52 have been amended to be in a form consistent with U.S. practice. No new matter has been added..

Claims 53-57 have been newly added to further define the claimed subject matter. New claim 54 is directed to "[a] method for treating a patient suffering from a

disease that is known to be treatable with a protein or polypeptide known to effectively treat the disease." Support for new claim 54 can be found throughout the specification and claims as originally filed. For example, please *see* page 4, lines 7 and 10-26 of the present specification. No new matter has been added.

New claims 55-57 are directed to "[a] method for extending the half-life of a protein or polypeptide in vivo." Support for new claims 55-57 can be found throughout the specification and claims as originally filed. For example, please *see* page 3, lines 27-29, and page 4, lines 1-6, of the present specification. No new matter has been added.

Applicants thank Examiner Kosar for conducting a telephone interview with the undersigned attorney on August 27, 2008 and on September 8, 2008. As discussed during the interviews, the pending method claims have been amended and new claim 54 has been added, where the claims are directed to "[a] method for treating a patient suffering from a disease that is known to be treatable with a protein or polypeptide known to effectively treat the disease...." New claims 55-57 have been added and are directed to "[a] method for extending the half-life of a protein or polypeptide in vivo...." As discussed during the telephone interview, new claims 55-57 recite an initial step of "providing...." Further, as discussed, the claims have been amended to properly recite the term "administering" in place of the term "administrating." Likewise, claims 47 and 50 have been amended to recite "administering to a patient in need thereof." No new matter has been added.

In view of the remarks set forth below, further and favorable consideration is respectfully requested.

I. At page 2 of the Official Action, claims 47, 50 and 51 have been rejected under 35 USC § 112, first paragraph.

The Examiner asserts that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with the claims. Specifically, the Examiner asserts that while the specification is "enabling for hemophilia, [it] does not reasonably provide enablement for any other diseases, disorders or conditions." *See* page 3 of the Official Action.

In view of the following, this rejection is respectfully traversed.

Claims 47 and 50 have been amended as discussed above. More specifically, claims 47 and 50 have been amended to recite, in part, a "method for treating a patient suffering from a disease that is known to be treatable with a protein or polypeptide known to effectively treat the disease," where the protein or polypeptide is selected from the group consisting of: (a) Factor VIIa, granulocyte colony-stimulating factor (G-CSF), granulocyte macrophage colony-stimulating factor (GM-CSF), interferon γ, glucagon-*like* peptide 1 (GLP-1) and Copaxone; or (b) proteins or polypeptides that comprise a consensus sequence of S/T-X-L/I/V-I/V/Q/S-S/T-X-X-E, where X may be any amino acid, and S, T, L, I, V, E and Q have their standard meanings.

The enablement provision of the Patent Act requires that the patentee provide a written description of the invention "in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same." 35 U.S.C. § 112, first paragraph (2000). The purpose of this requirement is to ensure that "the public knowledge is enriched by the

patent specification to a degree at least commensurate with the scope of the claims." *Nat'l Recovery Techs., Inc. v. Magnetic Separation Sys., Inc.*, 166 F.3d 1190, 1195-96 (Fed. Cir. 1999); *see also* Donald S. Chisum, 3 *Chisum on Patents* § 7.01 (2002).

Accordingly, the specification must provide sufficient teaching such that one skilled in the art could make and use the full scope of the invention without undue experimentation. *CFMT, Inc. v. Yieldup Int'l Corp.*, 349 F.3d 1333, 1338 (Fed. Cir. 2003); *Genentech, Inc. v. Novo Nordisk A/S*, 108 F.3d 1361, 1365 (Fed. Cir. 1997); *In re Wands*, 858 F.2d 731, 736-37 (Fed. Cir. 1988). "The key word is 'undue,' not experimentation.'" *Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988). Routine experimentation does not constitute undue experimentation. *See Johns Hopkins University v. Cellpro, Inc.,* 152 F.3d 1342 (Fed. Cir. 1998). That is, the specification need only teach those aspects of the invention that one skilled in the art could not figure out without undue experimentation. *See, e.g., Nat'l Recovery Techs.*, 166 F.3d at 1196 ("The scope of enablement . . . is that which is disclosed in the specification plus the scope of what would be known to one of ordinary skill in the art without undue experimentation."); *Wands*, 858 F.2d at 736-37 ("Enablement is not precluded by the necessity for some experimentation such as routine screening."). "Nothing more than objective enablement is required, and therefore it is irrelevant whether this teaching is provided through broad terminology or illustrative examples." *See In re Wright,* 999 F.2d 1557 (Fed. Cir. 1993).

Although the ultimate determination of whether one skilled in the art could make and use the claimed invention without undue experimentation is a legal one, it is based on underlying findings of fact. *CFMT*, 349 F.3d at 1337. Furthermore, "[w]hether undue

experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." *Wands*, 858 F.2d at 737.

Some of these considerations, commonly referred to as "the *Wands* factors," include "(1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims." *Id.; see also Amgen, Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1213 (Fed. Cir. 1991) (stating that the *Wands* factors "are illustrative, not mandatory" and that what is relevant to an enablement determination depends upon the facts of the particular case).

With regard to the presently pending claims, Applicants respectfully submit that the specification, figures, and experimental examples, provide ample guidance to the skilled artisan in view of the state of the art at the time the application was filed, to make and use the claimed subject matter without undue experimentation. Moreover, Applicants submit that diseases known to be treatable with a protein or polypeptide known to effectively treat the disease, where the protein or polypeptide is selected from the group consisting of: (a) Factor VIIa, granulocyte colony-stimulating factor (G-CSF), granulocyte macrophage colony-stimulating factor (GM-CSF), interferon γ, glucagon-*like* peptide 1 (GLP-1) and Copaxone; or (b) proteins or polypeptides that comprise a consensus sequence of S/T-X-L/I/V-I/V/Q/S-S/T-X-X-E, where X may be any amino acid, and S, T, L, I, V, E and Q have their standard meanings, are within the knowledge of one of ordinary skill in the art to which the present subject matter applies.

Additionally, Applicants respectfully submit that that the court in *In re Wright* held that nothing more than objective enablement is required, and therefore it is irrelevant whether this teaching is provided through broad terminology or illustrative examples.

Applicants note that a Declaration was submitted with the response filed on January 4, 2008, demonstrating that the claimed composition may be used to enhance the therapeutic effect of the proteins and polypeptides disclosed in the specification. In further support of Applicants position, Applicants provide herewith a copy of a second Declaration under 37 CFR § 1.132, executed by Dr. Moshe Baru, along with Annex A which describes experimental results that are discussed in the second Declaration. As indicated in paragraph 3 of the Declaration, Annex A describes the results of an experiment performed by Dr. Baru in which a composition comprising copaxone, that is prepared according to the presently claimed subject matter, is utilized for the treatment of acute colitis. As indicated by Dr. Baru at paragraph 3 of the Declaration, the treatment of colitis differs significantly from the treatment of hemophilia. *See* the Declaration at paragraph 3. Therefore, Applicants submit that the Declaration and attached Annex A provide evidence that the claims are sufficiently enabled for a scientist skilled in the relevant art to apply the claimed subject matter to other proteins and polypeptides.

According to Dr. Baru at paragraph 5 of the Declaration, the experimental results summarized in Annex A, demonstrate that the claims are sufficiently enable a scientist skilled in the relevant art to apply the claimed subject matter to other proteins and polypeptides. *See* the Declaration at paragraph 5. Further, Dr. Baru indicates that the results of the experiment provide a reasonable basis for the assumption that a

composition according to the presently claimed subject matter may be used to treat other diseases for which copaxone is known to be effective. *Id*. In this regard, Dr. Baru indicates that the results of the experiments described in Annex A may be used to provide a reasonable basis for the assumption that a formulation comprising copaxone and PEGLip, prepared according to the claims of the instant specification, improves the efficacy of copaxone in other inflammation and autoimmune diseases.

Regarding the acute colitis model, the following experiment was performed by Dr. Baru. C57Bl mice (8-10 weeks, 18-20 g) were randomized into 5 groups each including 9 animals. Acute colitis was induced by administration of DSS (MP Biomedicals, France, 2% wt./v) in the drinking water for 5 days followed by untreated water for additional 5 days. From initiation of the study, mice of three groups were injected daily subcutaneously with 200µl/ mice of Copaxone (Teva, Israel, 100 mg/kg), PEGylated liposomes (PEGLip) (4.5% weight lipids/volume), or PEGLip-Copaxone (4.5% weight lipids/volume, 100 mg Copaxone/kg). Groups of untreated mice and DSS-treated mice were used as normal and reference groups. Mice weight, overall diarrhea, rectal bleeding and survival were monitored daily. Ten days following initiation of the study, all mice were sacrificed and the intestine length was recorded. *See* page 1 of Annex A.

Measurements of column length at the end of the study indicated that a treatment by PEGLip-Copaxone was the most effective in protecting the colon. The average and median colon length of this group was 7.5 cm and 7.7 cm, respectively. Colon length of this group was not statistically different from that of control untreated mice. In contrast, the average and median colon length of standard Copaxone treated mice were 7.2 cm

and 7.4 cm, respectively. Colon length of this group was statistically different (p=0.049) from that of control untreated mice. *See* page 2 of Annex A.

The proportion of healthy or mildly affected mice (colon length >7.6) showed similarity between PEGLip-Copaxone treated mice and normal mice (81 and 89% healthy/mildly affected mice). However, groups treated by standard Copaxone or PEGLip only were found to be similar to the negative control DSS group mice (22-33% healthy/mildly affected mice). *See* page 2 of Annex A.

The weight gain of mice, treated with PEGLip-Copaxone, was similar to that of normal mice and statistically different from negative control DSS treated group (Fig. 3). Other groups including that of standard Copaxone treated mice were not statistically different from negative control DSS treated mice. *See* page 2 of Annex A.

The results of the experiments indicate that PEGLip improves the efficacy of copaxone in the treatment of acute colitis, as demonstrated in the 3 main parameters characterizing the disease: 1) Colon length; 2) Degree of disease (% of mice with a colon length of >7.6 cm); and 3) Weight gain.

Although the Examiner asserts, at page 13 of the Official Action, that the specification "does not provide any examples as where the therapeutic polypeptides are modified or conjugated to the surface of PEG or liposome," Applicants respectfully point out to the Examiner that it is not necessary to indicate which specific residue binds to which specific molecule, but merely to teach a person having skill in the art how to carry out the claimed subject matter as required by *In re Wright*. In addition, "[d]etailed procedures for making and using the invention may not be necessary if the description of the invention itself is sufficient to permit those skilled in the art to make and use the

invention." *See* MPEP at § 2164. The court in *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970), held that "[a]s long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement of 35 U.S.C. 112 is satisfied." *See* MPEP at § 2164.01(b).

Contrary to the Examiners assertion, the present specification describes and exemplifies, for example, at page 5, line 25 to page 6, line 8; page 11, lines 5 to 21; and page 13, lines 13-20, suitable coupling reactions as well as the binding of proteins/polypeptides to liposomes. More specifically, the paragraph bridging pages 5 and 6 of the present specification, recites the following with regard to coupling reactions:

> A ***variety of known coupling reactions may be used for preparing vesicle forming lipids derivatized with hydrophilic polymers***. For example, a polymer (such as PEG) may be derivatized to a lipid such as phosphatidylethanolamine (PE) through a cyanuric chloride group. Alternatively, a capped PEG may be activated with a carbonyl diimidazole coupling reagent, to form an activated imidazole compound. A carbamate-linked compound may be prepared by reacting the terminal hydroxyl of MPEG...to yield a p-nitrophenyl carbonate. This product is then reacted with ...to yield the intermediate carbamate. The hydroxyl groups of the diol are acylated to yield the final product. A similar synthesis...as described in WO 01/05873. ***Other reactions are well know and are described, e.g. in the aforementioned U.S. 5,013,556, whose contents are incorporated herein by reference***. (emphasis added)

The present specification, in Examples 1-8, at page 11, lines 5-21, describes the following with regard to binding of proteins/peptides to liposomes:

> ***Binding of proteins/peptides to PEGylated liposomes.*** We analyzed the binding of proteins and peptides to PEGylated liposomes by Surface Plasmon Resonance (SPR) measurement using a Biacore instrument .... We immobilized proteins/peptides on a CM5 sensor chip ..., then injected PEGylated liposomes or control liposomes of the same size...and concentration and measured and analyzed the binding of protein/peptide

> to the flowed intake liposomes. PEGylated liposomes composed of POPC and DSPE-PEG-2000 bind to FVIII (Fig. 1a). The binding was dependent on the PEG polymer attached to DSPE lipid since two types of control liposomes composed of POPC and POPC:DSPE did not bind to FVIII (Fig. 1a). In addition, the binding was specific to FVIII, since the PEGylated liposomes did not bind to human serum albumin (HSA) (Fig. 1b). Binding analysis of a representative curve (Fig. 1a) using a two-site binding model indicates that the PEGylated liposomes bind to two sites on FVIII with association rate constants..., dissociation rate constants ... and affinity constant ...values...(Table 1). (emphasis added)

Further, the present specification, in Examples 9-10, at page 13, lines 13-20, describes the following with regard to a formulation of FIX and G-CSF with PEGylated liposomes:

> Formulation of FIX and G-CSF with PEGylated liposomes. PEGylated liposomes were formulated with either FIX (Octanine, Octapharma) or G-CSF (ProSpec-Tany TechnoGene Ltd, Nes Ziona, Israel) by dissolving the protein with liposome solution (one ml liposome solution/200 units of FIX and 1 ml of liposome solution/10 µg of G-CSF). The vial was incubated on a SRT1 roller mixer rotate at 33 rpm, amplitude 16 mm (Stuart Scientific, Rehill, UK) for 10 minutes (G-CSF) or 60 minutes (FIX), at room temperature (20-25°C.).

In view of the foregoing and ***contrary to the Examiners assertion***, the present specification ***does describe and provide examples where the therapeutic polypeptides are modified or conjugated to the surface of PEG or liposomes.*** In summary, the presently claimed subject matter has been limited to a restricted list of proteins and to the diseases treatable by them. Thus, Applicants assert that the claimed subject matter is fully enabled by the specification within the meaning of 35 USC § 112, first paragraph.

In view of the remarks, the Declaration and supporting documents submitted herewith, together with the previously filed Declaration, Applicants respectfully submit that the specification, figures, and experimental examples, provide ample guidance to

the skilled artisan in view of the state of the art at the time the application was filed, to make and use the claimed invention without undue experimentation. In particular, the pending claims are enabled for at least the following four (4) different polypeptides and three (3) different diseases:

a. Factor IX (examples 9-10 of the specification);
b. G-CSF (examples 9-10 of the specification);
c. Factor VIIa (example 13 of the specification);
d. G-CSF for the treatment of neutropenia (1st Declaration);
e. G-CSF for mobilization of stem cells into peripheral blood (1st Declaration); and
f. Copaxone for treatment of inflammatory bowel disease (IBD) (2nd Declaration).

Applicants note that the above list of examples is not intended to be exhaustive, and the scope of the claims is not limited to the above examples.

Regarding new claims 55-57 directed to a "method for extending the half-life of a protein or polypeptide in vivo," Applicants note that the Examiner, at pages 12 and 13 of the outstanding Official Action, appears to allege that claims broadly drawn to a method of treatment would not be enabled, while claims "drawn to extending the life of the composition" would be enabled. *See* the outstanding Official Action at page 13.

Therefore, Applicants submit that the present specification enables the skilled artisan to make and use the full scope of claims 47, 50 and 51 within the meaning of 35 USC § 112, first paragraph. Thus, the Examiner is respectfully requested to withdraw this rejection.

II. At page 14 of the Official Action, claims 28-42 and 46 are rejected under 35 USC § 112, first paragraph.

The Examiner asserts that the specification does not clearly define or provide examples of what qualifies as compounds of the claimed invention. *See* page 16 of the Official Action. Further, the Examiner states that a protein or polypeptide having a consensus sequence S/T-X-L/I/V-I/V/Q/S-S/T-XX-E, where X may be any amino acid lead to many different peptide consensus sequences. *See* page 18 of the Official Action.

In view of the following, this rejection is respectfully traversed.

The test under 35 U.S.C. § 112, first paragraph, for determining compliance with the written description requirement is whether the application clearly conveys that an applicant has invented the subject matter which is claimed. *In re Barker*, 194 USPQ 470, 473 (CCPA 1977); MPEP 2163. Also, the applicant must convey to the public what the applicant claims as the invention so that the public may ascertain if the patent applicant claims anything in common use or already known. MPEP § 2163. Lastly, the specification must convey that the applicant was in possession of the invention. MPEP § 2163. The Examiner is respectfully reminded that the Examiner has the initial burden of presenting evidence or reasons why persons skilled in the art would not recognize in an applicant's disclosure a description of the invention defined by the claims. *In re Wertheim*, 191USPQ 90, 98 (CCPA 1976).

Applicants respectfully submit that the specification complies with the written description requirement for presently pending claims 28-42 and 46. Applicants note that independent claim 28 has been amended to recite specific proteins described in the

specification. Specifically, claim 28 now recites the following proteins or polypeptides: Factor VIIa, granulocyte colony-stimulating factor (G-CSF), granulocyte macrophage colony-stimulating factor (GM-CSF), interferon γ, glucagon-*like* peptide 1 (GLP-1) and Copaxone.

Regarding the Examiner's assertion that the consensus sequence includes a great number of possibilities, a simple calculation shows that the consensus sequence substantially limits the number of possible combinations by 67,368 times.

a. Random possible combinations of amino acids in 8 amino acid sequence: 20^8 = **25.6×10^9**.

b. No. of possible combinations of amino acids in the consensus sequence S/T-X-L/I/V-I/V/Q/S-S/T-X-X-E are: 2 x 20 x 3 x 4 x 2 x 20 x 20 x 1 = **3.8×10^5**.

c. $25.6 \times 10^9 / 3.8 \times 10^5$ = **67,368**.

Thus, the consensus sequence is limited to 0.000015 of all possible sequences. Applicants assert that this is a description of the claimed subject matter and not an indication of a result that one might achieve.

Accordingly, Applicants submit that, as amended, claims 28-42 and 46, satisfy the written description requirement of 35 USC § 112, first paragraph. Thus, the Examiner is respectfully requested to withdraw this rejection.

III. At page 19 of the Official Action, claims 28-32, 36-37 and 39-43 are rejected under 35 USC § 102(b) as being anticipated by Baru et al.

The Examiner asserts that Baru et al. (WO 99/55306) teach a pharmaceutical composition for parenteral administration comprising a therapeutically effective amount of a protein or polypeptide and substantially neutral colloidal particles. *See* page 20 of the Official Action.

In view of the remarks set forth herein, this rejection is respectfully traversed.

The test for anticipation is whether each and every element as set forth is found, either expressly or inherently described, in a single prior art reference. Verdegaal Bros. v. Union Oil Co. of California, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987); MPEP § 2131. The identical invention must be shown in as complete detail as is contained in the claim. Richardson v. Suzuki Motor Co., 9 USPQ2d 1913, 1920 (Fed. Cir. 1989); MPEP §2131. The elements must also be arranged as required by the claim. In re Bond, 15 USPQ2d 1566 (Fed. Cir. 1990).

As discussed above, amended claim 28 recites "[A] pharmaceutical composition for parenteral administration comprising a therapeutically effective amount of a protein or polypeptide non-covalently bound to one or more colloidal particles, the one or more colloidal particles comprising approximately 1-20 mole percent of an amphipathic lipid derivatized with a biocompatible hydrophilic polymer, wherein the protein or polypeptide is selected from the group consisting of: (a) Factor VIIa, granulocyte colony-stimulating factor (G-CSF), granulocyte macrophage colony-stimulating factor (GM-CSF), interferon γ, glucagon-*like* peptide 1 (GLP-1) and Copaxone; or (b) proteins or polypeptides that comprise a consensus sequence of S/T-X-L/I/V-I/V/Q/S-S/T-X-X-E, where X may be any amino acid, and S, T, L, I, V, E and Q have their standard meanings; wherein the protein or polypeptide is not Factor VIII (FVIII), and the protein or polypeptide is not encapsulated in the one or more colloidal particles." Claims 29-32, 36-37 and 39-42 depend, either directly or indirectly, from claim 28. Claim 43 has been canceled.

In contrast, Baru et al. is directed to a pharmaceutical composition for parenteral administration comprising a therapeutically effective amount of a protein or polypeptide and substantially neutral colloidal particles. The particles according to Baru et al. comprise approximately 1-20 mole percent of an amphipathic lipid derivatized with a biocompatible hydrophilic polymer which carries substantially no net charge. According to Baru et al. the protein or polypeptide is capable of externally binding the colloidal particles, or is capable of binding polyethylene glycol, and is not encapsulated in the colloidal particles. Baru et al. describes that a preferred protein is factor VIII, whose half-life is extended and which is protected from serum inhibitor antibodies by injecting it as a component of the composition. *See* the Abstract, Baru et al.

Applicants respectfully submit that, as amended, claim 28 is not anticipated by Baru et al. More specifically, amended claim 28 now recites the specific proteins or polypeptides in paragraphs (a) and (b). Baru et al. does not describe any of the specific proteins or polypeptides recited in paragraphs (a) and (b) of amended claim 28.

Accordingly, Applicants submit that Baru et al. do not teach each and every element of amended claim 28, as required for anticipation under 35 USC § 102(b). Therefore, Applicants respectfully request that the Examiner reconsider and withdraw the rejection of claims 28-32, 36-37 and 39-42 under 35 USC § 102(b).

IV. At page 21 of the Official Action, claims 28-29, 32-33 and 39-43 are rejected under 35 USC § 102(e) as being anticipated by Zalipsky et al.

The Examiner asserts that Zalipsky et al. (U.S. Patent No. 6,586,002) teach a liposome composition comprising small, surface-bound effector molecules, and

liposomes have a surface layer of hydrophilic polymer chains, for enhanced circulation time in the blood stream. *See* page 21 of the Official Action.

In view of the remarks set forth herein, this rejection is respectfully traversed.

The test for anticipation as discussed above in Section III is incorporated herein in its entirety.

As discussed above, amended claim 28 recites "[A] pharmaceutical composition for parenteral administration comprising a therapeutically effective amount of a protein or polypeptide non-covalently bound to one or more colloidal particles, the one or more colloidal particles comprising approximately 1-20 mole percent of an amphipathic lipid derivatized with a biocompatible hydrophilic polymer, wherein the protein or polypeptide is selected from the group consisting of: (a) Factor VIIa, granulocyte colony-stimulating factor (G-CSF), granulocyte macrophage colony-stimulating factor (GM-CSF), interferon γ, glucagon-*like* peptide 1 (GLP-1) and Copaxone; or (b) proteins or polypeptides that comprise a consensus sequence of S/T-X-L/I/V-I/V/Q/S-S/T-X-X-E, where X may be any amino acid, and S, T, L, I, V, E and Q have their standard meanings; wherein the protein or polypeptide is not Factor VIII (FVIII), and the protein or polypeptide is not encapsulated in the one or more colloidal particles." Claims 28-29, 32-33 and 39-42 depend, either directly or indirectly, from claim 28. Claim 43 has been canceled.

In contrast, Zalipsky et al. is directed to a liposome composition comprising small, surface-bound effector molecules. The liposomes according to Zalipsky et al. have a surface layer of hydrophilic polymer chains, for enhanced circulation time in the

bloodstream. Additionally, the effector molecules according to Zalipsky et al. are attached to the distal ends of the polymer chains. See the Abstract, Zalipsky et al.

Applicants respectfully submit that, as amended, claim 28 is not anticipated by Zalipsky et al. More specifically, claim 28 now defines the bond between the protein or polypeptide and colloidal particle as a "non-covalent" bond. In contrast to the presently claimed subject matter, Zalipsky describes liposome compositions in which the effector molecule is ***covalently*** bound to the liposome carrier. See Zalipsky et al. at Col. 3, lines 1-2; Col. 3, line 65 to Col. 4, line 9 (description of Figs. 9-11); Col. 5, lines 33-44; Col. 11, lines 25-35; and Col. 24, lines 30-67 (Example 6).

Accordingly, Applicants submit that Zalipsky et al. do not teach each and every element of amended claim 28, as required for anticipation under 35 USC § 102(b). Therefore, Applicants respectfully request that the Examiner reconsider and withdraw the rejection of claims 28-29, 32-33 and 39-42 under 35 USC § 102(e).

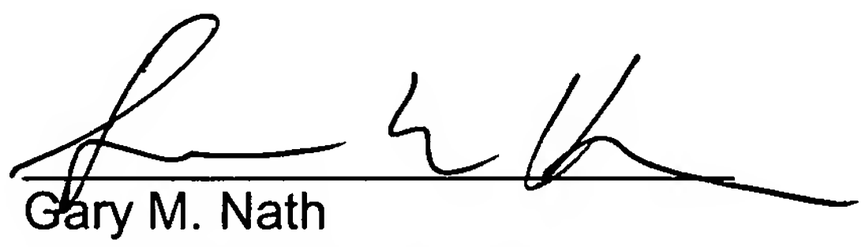
CONCLUSION

In view of the foregoing, Applicant submits that the application is in condition for immediate allowance. Early notice to that effect is earnestly solicited. The Examiner is invited to contact the undersigned attorney if it is believed that such contact will expedite the prosecution of the application.

In the event this paper is not timely filed, Applicants petition for an appropriate extension of time. Please charge any fee deficiency or credit any overpayment to Deposit Account No. 14-0112.

Respectfully submitted,

THE NATH LAW GROUP



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